

REMARKS

Applicant respectfully requests entry of the amendments hereinabove, reconsideration of the Final Office Action mailed on November 3, 2003 and allowance of the application.

Claims 1-7 and 9-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The rejection states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention.

The rejection states that in response to the rejection of claims 1-8 and 11 under 35 U.S.C. 102(b), as being anticipated by Lee et al., Applicant amended the claims. The rejection also states that newly amended claims now recite that an estrogen agonist/antagonist is not co-administered and Applicant states in page 4, lines 21-27 of the Amendment "Applicant submits that this amendment is fully supported. Support for this amendment may be found in claim 1 as originally filed. In addition, Applicant submits that the literal basis for such amendment is not required to be found in the specification (the claims phrase need not be "in haec verba" in the specification [citing case law]".

The rejection states that Applicant is correct that in order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in "haec verba" support for the claimed subject matter in the claims. The rejection states that, however, the disclosure must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. The rejection reasons that when Applicant adds a claim or otherwise amends his specification after the original filing date, the new claims or other added material must find support in the original specification.

The rejection states that when all evidences in the original disclosure are considered and carefully reviewed, the newly amended claims fail to find support in the original specification.

The rejection states that the specification discloses as an embodiment of the invention that PDE5 inhibitors can be combined with one or more additional active

agents for the treatment of PD in patients with normal erectile function. The rejection also states that the specification provides examples of various suitable agents for the claimed invention including estrogen agonist/antagonists (page 16, line 14, thru page 19, line 15). Specifically, in page 17, lines 25-29, raloxifene or lasofoxifene and (-)-cis-6-phenyl-5-{4-(2-pyrrolidin-1-yl-ethoxy)-phenyl}-5,6,7,8-tetrahydronaphthalene-2-ol are disclosed as preferred estrogen agonists and/or estrogen antagonists.

The rejection states that it would have been clear that the claimed invention can be practiced with the PDE5 in combination with other active agents disclosed in the specification including estrogen agonist/antagonist, not excluding estrogen agonist/antagonist as are in newly amended claims.

Applicant traverses the rejection of the claims (as amended) under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicant reiterates that the literal basis for such amendment is not required to be found in the specification (the claim phrase need not be "*in haec verba*" in the specification *In Re Wright* 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989); *Crowne Operations, Int'l, Inc. v. Solutia, Inc.* 289 F.3d 1367, 1376 (Fed. Cir. 2002). Applicant submits that it is well settled that an inventor may excise the prior art from the claim and still satisfy the written description requirement of section 112, first paragraph *In re Johnson*, 194 U.S.P.Q.187 (C.C.P.A. 1977). Thus, it is a perfectly legitimate procedure for an inventor to claim less than the full scope of his disclosure since it is for an inventor to decide what bounds of protection he will seek (see *In re Wertheim* 191 U.S.P.Q. 90 (C.C.P.A. 1976)). See also *In re Driscoll* 195 U.S.P.Q. 434 CCPA 1977 which cites the following case.

Engineering Development Laboratories v. Radio Corp. of America 68 USPQ 238 241-242 (CA2 1946).

Judge Learned Hand

"If, when [applicants] yield any part of what they originally believed to be their due, they substitute a new "invention", only two courses will be open to them: they must at the outset either prophetically divine what the art contains, or they must lay down a barrage of claims, starting with the widest and proceeding by the successive incorporation of more and more detail, until all combinations have been exhausted

less than 10 nanomolar (column 23, lines 51-54); and the cGMP PDE_v inhibitors are selective over PDE_{iii}, more preferably over PDE_{III}, and PDE_{iv} (column 23, lines 62-65). The rejection also states that the reference also discloses that the claimed composition is preferably administered in different dosage forms including oral administration (column 41, lines 21-23).

The rejection notes that since the instant claims recite "comprising" language, the reference clearly anticipates the claimed invention.

Applicant traverses the rejection of the claims (as amended) under 35 U.S.C. 102(e) in light of Lee et al.

The Court of Appeals for the Federal Circuit, in ruling on the standard for anticipation under 35 U.S.C. §102(b), stated

[i]t is elementary that an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice or device.

In re Donohue, 226 U.S.P.Q. 619, 621 (1985); and "...exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference." Atlas Power Co. v. E. I. duPont DeNemours & Co., 224 U.S.P.Q. 409, 411 (1984).

As amended Applicant submits that his claims are not anticipated since they exclude the co-administration of an estrogen agonist/antagonist.

Applicant also submits that his claims are not obvious in light of Lee et. al. since Applicant submits that Lee et. al. does not provide the motivation to utilize a PDE5 inhibitor (without co-administering an estrogen agonist/antagonist) to treat premature ejaculation. The only statement regarding the use of a PDE5 inhibitor alone is provided on column 5, lines 32-39. "More recently cGMP PDE inhibitors capable of inhibiting type V phosphodiesterase (cGMP PDE_v) have been found to be effective for the treatment of impotence, importantly by oral administration." Applicant submits that the treatment of impotence is quite different from the treatment of premature ejaculation. Applicant submits that there is no motivation to modify the teachings of Lee et al. to achieve Applicant's claimed invention. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. "The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the

which can by any possibility succeed. The first is an impossible task; the second is a custom already more honored in the breach than in the observance, and its extension would only increase that surfeit of verbiage which has for long been the curse of patent practice, and has done much to discredit it. *It is impossible to imagine any public purpose which it could serve. [Emphasis added]*

Applicant reiterates that the amendment is fully supported. Support for this amendment may be found in claim 1 as originally filed and as further discussed hereinafter. In addition, Applicant notes the acknowledgment of the Examiner that the specification "provides examples of various suitable agents for the claimed invention including estrogen agonist/antagonist (page 16, line 14, thru page 19, line 15). Specifically, in page 17, lines 25-29, raloxifene or lasofoxifene and (-)-cis6-phenyl -5-{4-(2-pyrrolidin-1-yl-ethoxy)-phenyl}-5,6,7,8-tetrahydronaphthalene-2-ol are disclosed as preferred estrogen agonists and/or estrogen antagonists." Accordingly, the rejection states that estrogen agonist/antagonists are disclosed as combination agents. However, the rejection appears to presume that the claimed invention would be practiced with the combination estrogen agonist/antagonists agent, but not without the combination agent. This is incorrect since the specification clearly contemplates the use of PDE5 inhibitors without such agents ("the PDE5 inhibitors **may** also be combined with one or more additional active agents for treating PE", specification, page 16, lines 14-15) (emphasis added). Applicant submits that the use of the term **may** with reference to the use of combination agents clearly indicates that one embodiment of the invention is that the PDE5 inhibitors **may be used without one or more additional agents** (the estrogen agonist/antagonists noted by the Examiner being one of the additional combination agents).

Claims 1-8 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al. (US 65122002 B2).

The rejection states that Lee teaches the co-administration of estrogen agonists/antagonists and a cGMP PDE_v inhibitor (e.g., sildenafil) for the treatment of premature ejaculation (column 21, lines 19-23; claims 3 and 5). The rejection also states that the reference discloses that the cGMP PDE_v inhibitors have an IC₅₀ for PDE_v at less than 100 nonomolar, more preferably, at less than 50 nanomolar, more preferably still at

desirability of the modification." In re Laskowski, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

The rejection does not detail reasoning that provides the motivation to modify the prior art and thus the rejection does not present a *prima facie* case of obviousness.

Claims 1-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Wilson et al. (US 6403597 B1).

The rejection states that Wilson teaches the use of type V phosphodiesterase inhibitors such as sildenafil for treating premature ejaculation (abstract; column 4, lines 9-18; claims). The rejection also states that the reference also teaches the claimed oral administration (claims 15, 17-19, 21, 40-44 of US '597) as required in claim 8 and the claimed dosage amount of phosphodiesterase inhibitors (e.g., sildenafil citrate), in the range of about 1 mg to about 250 mg, typically in the range of about 15 mg. to about 100 mg (column 22, line 65 thru column 23, line 7), as required in claims 9-10.

The rejection states that although the reference is silent about "PDE5 inhibitor has an IC 50 against the PDE5 enzyme of less than 100 nanometer" in claim 3; "PDE5 inhibitor has selectivity over PDE3 of greater than 100 fold" in claim 4; "PDE5 inhibitor has selectivity over both PDE3 and PDE4 of greater than 100 fold" in claim 5; and "PDE5 inhibitor has an IC 50 against the PDE5 less than 100 nM and a selectivity over PDE3 of greater than 100 fold" in claim 6, such characteristics or properties are deemed to be inherent to the composition, i.e., it was always there.

The rejection states that in Applicant's Amendment and Response to the previous Office Action, Applicant stated that the claims are not anticipated since Wilson et al. does not teach the oral administration of a PDE5 inhibitor before Applicant's priority file date. The rejection responds that the term "orally" is defined as "by, with, or in, the mouth" (Webster's Revised Unabridged Dictionary 1913) and generally means "(of drugs) administered by mouth" in the art. The rejection concludes that the term "orally" given a reasonably broader interpretation, encompasses the sublingual tablet and buccal dosage form disclosed in the Wilson et al. application. The rejection concludes that the reference anticipates the claimed invention.

Applicant traverses the rejection of the claims (as amended) under 35 U.S.C. 102(e) in light of Wilson et al.

Preliminarily, the claims have been amended to recite that the administration is oral "but not including buccal or sublingual". Applicant submits that this amendment is fully supported. Support for this amendment may be found in claim 8 as originally filed and page 11, line 9 and page 9, lines 9-13 which recite "orally, bucally or sublingually".

Applicant refers to the case law cited above relevant to the allowable claim amendments e.g., *In Re Wright* 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989).

Further, Applicant submits that, in particular, the specification, page 9, lines 9-13 which recite "orally, bucally or sublingually" provides support since it refers to the three administration modes in the alternative (i.e., or) thus indicating that the administration could be oral, but, without buccal or sublingual administration..

The Court of Appeals for the Federal Circuit, in ruling on the standard for anticipation under 35 U.S.C. §102(b), stated

[i]t is elementary that an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice or device.

In re Donohue, 226 U.S.P.Q. 619, 621 (1985); and "...exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference." Atlas Power Co. v. E. I. duPont DeNemours & Co., 224 U.S.P.Q. 409, 411 (1984).

As amended, Applicant submits that his claims are not anticipated since Wilson et al. does not teach the oral administration of a PDE5 inhibitor before Applicant's priority file date of November 20, 2000. Thus, Wilson et al. does not teach each element of the claimed invention. Specifically, while Wilson et al. application serial number 09/888,250 filed on June 21, 2001 does disclose the oral administration of a PDE5 inhibitor for the treatment of premature ejaculation, the parent application (Wilson et al. application serial no. 09/467,094 filed December 10, 1999) does not disclose the oral administration of a PDE5 inhibitor for the treatment of premature ejaculation. Accordingly, as of December 10, 1999 the only administration method was transmucosal (e.g., buccal, sublingual, rectal) application serial no. 09/467,094 page 8, line 29- page 9, line 8. Since Applicant's application has a filing date that is prior to the earliest Wilson et al. application that teaches oral administration Wilson et al. is not an effective reference under 35 U.S.C. 102(e). This is because the invention was not described in a patent that was filed prior to Applicant's invention thereof as evidenced by Applicant's November 20, 2000 priority filing date.

Applicant notes that his claims as amended clearly do not encompass the terms buccally or sublingually.

Applicant also submits that his claims are not obvious in light of Wilson et. al. since Applicant submits that Wilson et. al. does not provide the motivation to administer a PDE5 inhibitor to treat premature ejaculation by an oral route. The 09/467,094 application is clearly directed to transmucosal administration routes and never suggests a different method of administration. Applicant submits that oral administration is quite different from transmucosal (buccal or sublingual) administration.

First, oral administration is unobvious in light of the Wilson et al which does not suggests oral administration. Second, Applicant strongly submits that by emphasizing local administration one skilled in the art would recognize that the reference impliedly teaches away from oral administration (the normal and preferred method of pharmaceutical administration). Restated, the only logical conclusion from Wilson et al.'s emphasis on local administration is that the normal preferred oral administration is not available as a mode of administration.

Applicant further submits that there is no motivation to modify the teachings of Wilson et al. to achieve Applicant's claimed invention. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. "The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." In re Laskowski, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

The rejection does not detail reasoning that provides the motivation to modify the prior art and thus the rejection does not present a *prima facie* case of obviousness.

Again, oral administration is nowhere suggested or disclosed in Wilson et al. in animals or humans, and Applicant submits that the fact that a compound can be administered by a particular route for one indication does not necessarily mean that that mode of administration will be useful for a different indication. In support of this argument, Applicant encloses a copy of the following Exhibit:

Exhibit A - Meinhardt et al., Internat. J. Impot. Res, 1997, 9, 17-26.

With reference to the nonobviousness of oral administration, Exhibit A discloses (see page 21 bottom left column) that

"Several vasodilators have a relaxing effect on the corporal tissue when applied intracavemosally or even topically, but this effect is not obvious when these drugs are taken orally...".

The above quotation demonstrates that just because a compound is known to be orally administrable for one indication does not automatically mean that it is administrable orally for other indications. Simply, because many vasodilators are known for oral administration that does not mean they will automatically work to relax corporal tissue via oral administration, as illustrated by the above quotation. Indeed in Meinhardt, compounds known for administration by one route were inappropriate for administration by a different route even for the same indication. The same argument applies with equal force to Applicant's compounds--just because they were known for oral administration for the treatment of cardiovascular condition or impotence, the conclusion that prior to Applicant's invention one would have believed there was a reasonable likelihood of success that they would work orally to treat premature ejaculation is unwarranted.

Further, even allowing, *arguendo*, that any such suggestion or motivation were found in Wilson, the references provide no reasonable expectation of success.

Thus, the law is emphatic that "obvious to try" is NOT the test of obviousness under 35 U.S.C. §103. American Hospital supply Corp. v. Travenol Laboratories, Inc., 223 USPQ 577, 582 (Fed. Cir. 1984). The Federal Circuit has explained the proper test:

The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out **and would have a reasonable likelihood of success**, viewed in light of the prior art. **Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure** (emphasis added).

In re Dow Chemical Co., 5 USPQ.2d 1529, 1531 (Fed. Clr. 1988); Amgen, Inc. V. Chugai Pharmaceutical Co. Ltd. 18 USPQ.2d 1016. 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

In light of the arguments concerning the Meinhardt reference Wilson clearly provides no reasonable expectation or likelihood of success. Again, even if an argument

could be made that the art provides a suggestion to explore the oral administration of PDE5 inhibitors to premature ejaculation, this amounts, perhaps, to inviting experimentation, i.e., to perhaps making testing a PDE5 more obvious to try, which again is manifestly not the proper standard for patentability.

Applicant notes that the previous rejection of claims 1-11 under 35 U.S.C. 103(a) as being unpatentable over Doherty, Jr. et al. (US 6037346 A), if necessary, and further view of Crenshaw et al (US 5276042) and Crenshaw et al (5151448) and/or Bick (US 4940731) has not been maintained.

Applicant requests allowance of the application.

Respectfully submitted,

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